Conclusions: These ML algorithms accurately predicted irAEs in melanoma patients. Key predictors of irAE included increasing age, female gender and exposure to combination therapy or pembrolizumab. Future work will aim to externally validate these models and incorporate them into ICI drug development trials to prospectively predict which patients will develop irAEs. Our models can also be used as tools to support informed decision-making between clinicians and patients considering starting, stopping or continuing ICI therapy.

Legal entity responsible for the study: The authors.

Funding: Curenetics.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.esmoop.2025.104158

4P Machine learning-based prediction of survival in patients with metastatic renal cell carcinoma receiving first-line immunotherapy

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Background: Immunotherapy has significantly improved survival outcomes for patients with metastatic renal cell carcinoma (mRCC). However, considerable variability exists in patient survival. Machine learning (ML) models offer an opportunity to harness diverse patient data to predict survival outcomes and tailor treatment strategies. This study aimed to develop ML models to predict the overall survival (OS) in mRCC patients receiving first-line immunotherapy.

Methods: We analysed 4895 mRCC patients from the National Cancer Database who received first-line immunotherapy since 2015. Fifteen features were selected based on the univariate Cox regression for OS, including demographics, Charlson-Deyo Score, tumour side, grade, lymph vascular invasion, and prior surgery or radiotherapy. Missing values were imputed using K-Nearest Neighbors. The data was split into training (70%) and testing (30%) sets. Classification and regression models were compared using hyperparameter tuning and 5-fold cross-validation. The SMOT technique addressed class imbalance.

Results: The 1-year and 3-year OS were 32.7% and 9.9%, respectively. Among the classification models, CatBoost demonstrated the best performance, with an area under curve (AUC) of 0.87, followed by LightGBM (0.86), XGBoost (0.86), and Decision Tree (0.86). The Decision Tree model achieved the highest F1 score (0.57), indicating a good balance between precision and recall. However, simpler models like Naive Bayes showed lower performance across all metrics. In the regression task, CatBoost also achieved the best performance, with a Mean Squared Error (MSE) of 115.5 and an R^2 score of 0.52, indicating robust predictive accuracy. Feature importance analysis showed that tumour grade was the most significant predictor, followed by prior surgery and patient age. Socioeconomic factors, such as insurance status and facility type, also contributed significantly to the outcomes, while race had minimal predictive importance in this cohort.

Conclusions: Ensemble methods, particularly CatBoost, show superior performance in predicting mRCC outcomes. Tumour grade, surgery, and patient age emerged as key predictors.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.esmoop.2025.104159

5P Radiomic prediction of prognostic outcomes and immune profile in breast cancer: Focus on STAT3 expression

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Background: The identification of non-invasive prognostic stratification methods for breast cancer and the discovery of reliable biomarkers for precision therapy are of paramount importance. STAT3—a pivotal transcription factor integral to the regulation of numerous cellular processes, has been shown to be correlated with overall survival (OS) and can be predicted through radiomics potentially.

Methods: The research cohort of 101 patients with matched RNA-seq data from TCGA and DCE-MRI from TCIA. To evaluate STAT3 expression and prognosis, Kaplan-Meier survival analysis, Cox regression analysis, and subgroup analyses were implemented. Functional enrichment analysis and immune cell infiltration examination were conducted. Breast cancer IHC images from HPA database were analyzed by DIA via QuPath software. Radiomic features were extracted from DCE-MRI images using pyradiomics toolset. A predictive radiomics model for STAT3 expression was constructed by LASSO regression and binary logistic regression. The efficacy of the model was assessed by ROC curves, PR curves, goodness-of-fit test, and DCA. The correlation between Rad-scores and immune-related gene expression levels from ImmPORT database was examined by Spearman's rank correlation coefficient.

Results: Our findings indicated that reduced STAT3 expression in patients with breast cancer was associated with a poorer prognosis [Hazard ratio (HR) = 1.927, 95% CI: 1.369-2.712, $p < 0.001$]. STAT3 expression was significantly lower in tumor tissue compared to normal breast tissue ($p < 0.001$). The radiomic model exhibited an area under the curve (AUC) of 0.861 in the training set and 0.742 in the validation set ($p = 0.348$). PR, calibration and DCA curves all confirmed a robust predictive capability of the model. Furthermore, Rad-scores were found to be correlated with STAT3 expression and OS; higher Rad-scores were associated with increased STAT3 expression ($p < 0.001$) and shorter OS ($p = 0.033$).

Conclusions: The radiomics model based on DCE-MRI has the potential to non-invasively forecast STAT3 expression preoperatively, thereby providing novel insights into the survival prognosis and personalized treatment strategies for patients with breast cancer.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.esmoop.2025.104160

6P vAO - Variant Annotator for OncoKB: A simplified interface to identify targeted therapies for somatic tumors

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Background: Genomic variants from somatic tumors play a vital role in both therapy response and resistance. Annotating and understanding such actionable variants becomes a crucial step in precision oncology research to plan targeted therapeutic strategies. We have built a user-friendly program, vAO: Variant Annotator for OncoKB, which performs an API-based identification of targetable variants in large datasets.

Methods: vAO is a standalone executable file deployable on any Windows operating system computer. It supports two annotation workflows: genomic coordinate-based and amino acid alteration-based annotation using user-provided files in VCF, and Microsoft Excel formats, respectively. The number of variants to be annotated is user-defined, ranging from a few variants to complete exome sequences in the input file. Users can opt for their preferred genome build (GRCh37/38) and annotation mode, input the OncoKB™ API token, and select files to perform the analysis with a simple and intuitive interface.

Results: The output of this interface is provided to the user as an Excel spreadsheet for easy exploration and downstream analysis. The output files provide insights into the oncogenicity of the variant, level of sensitivity, targeted drugs available, sites of impact, and description of the variants, irrespective of the annotation workflows. The genomic coordinate-based annotation provides additional information on the impacted genes and the amino acid consequences.

Conclusions: vAO eliminates the need for programming expertise, enabling rapid and efficient annotation of large genomic variant datasets from somatic tumors. The automated workflow facilitates the identification of targeted therapies based on an individual's genomic profile.

Legal entity responsible for the study: Indian Institute of Technology Hyderabad.

Funding: Junior Research Fellowship (DBT/2020/IIT-H/1452) - Department of Biotechnology, Government of India and Indian Institute of Technology Hyderabad.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.esmoop.2025.104161